Opportunity for Biophotonics in Future Healthcare

Rajesh Kumar

May 04, 2017

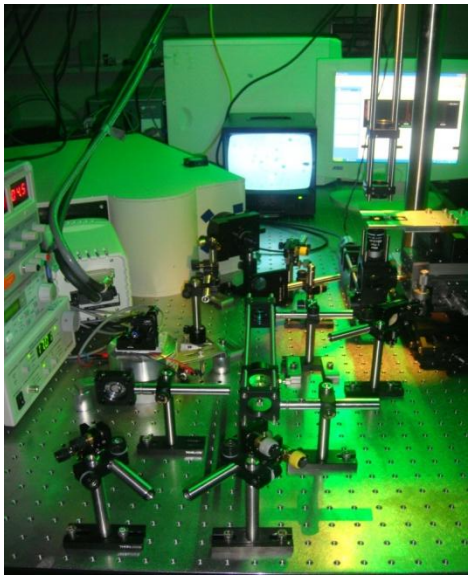
Jet Propulsion Laboratory, California Institute of Technology, USA
and
Norwegian University of Science and Technology (NTNU), Norway

Jet Propulsion Laboratory
California Institute of Technology

© 2017. All rights reserved

Introduction

Biophotonics
-uses light to view and analyse tissues and cells
-detect, diagnose and treat diseases
e.g., cancer, heart disease, Alzheimer's…



Interaction of light with matter
- absorption
- scattering
- fluorescence

Due to enhancement in life expectancy, the population of older people are increasing but, they lives more years with disability.
-older population, lower quality of life, higher costs
-demand of new tools to cure disease before they go to chronicity

Role of biophotonics in the future of clinical diagnostics
- High speed
- low cost
- non-invasiveness

Osteoarthritis (OA)

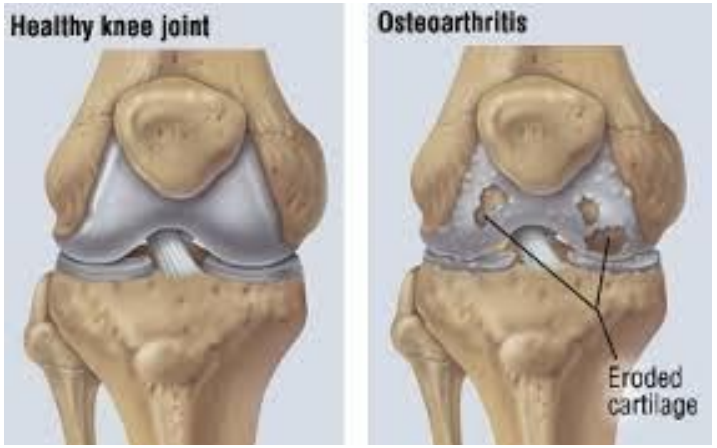
- ❑ A complex musculoskeletal disorder
- ❑ A leading cause of individual and socioeconomic burden
- ❑ Fastest increasing health condition

Relatively little is known about the underlying mechanism of OA

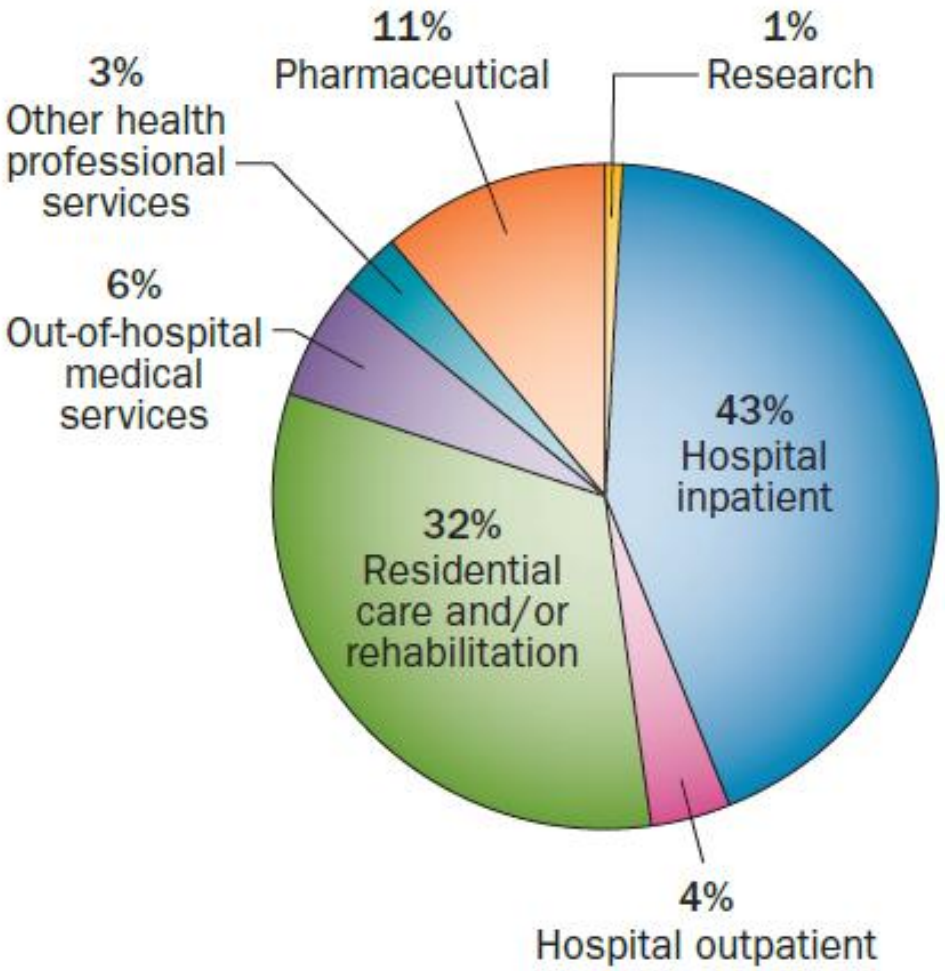
- Inherent heterogeneity
- Slow evolution of the joint disorder
- Lack of accurate characterization method

Clinical features of Osteoarthritis

- Pain in the joints
- Stiffening of the joints
- Restricted movement of the joint
- Bony swelling, crepitus and deformities

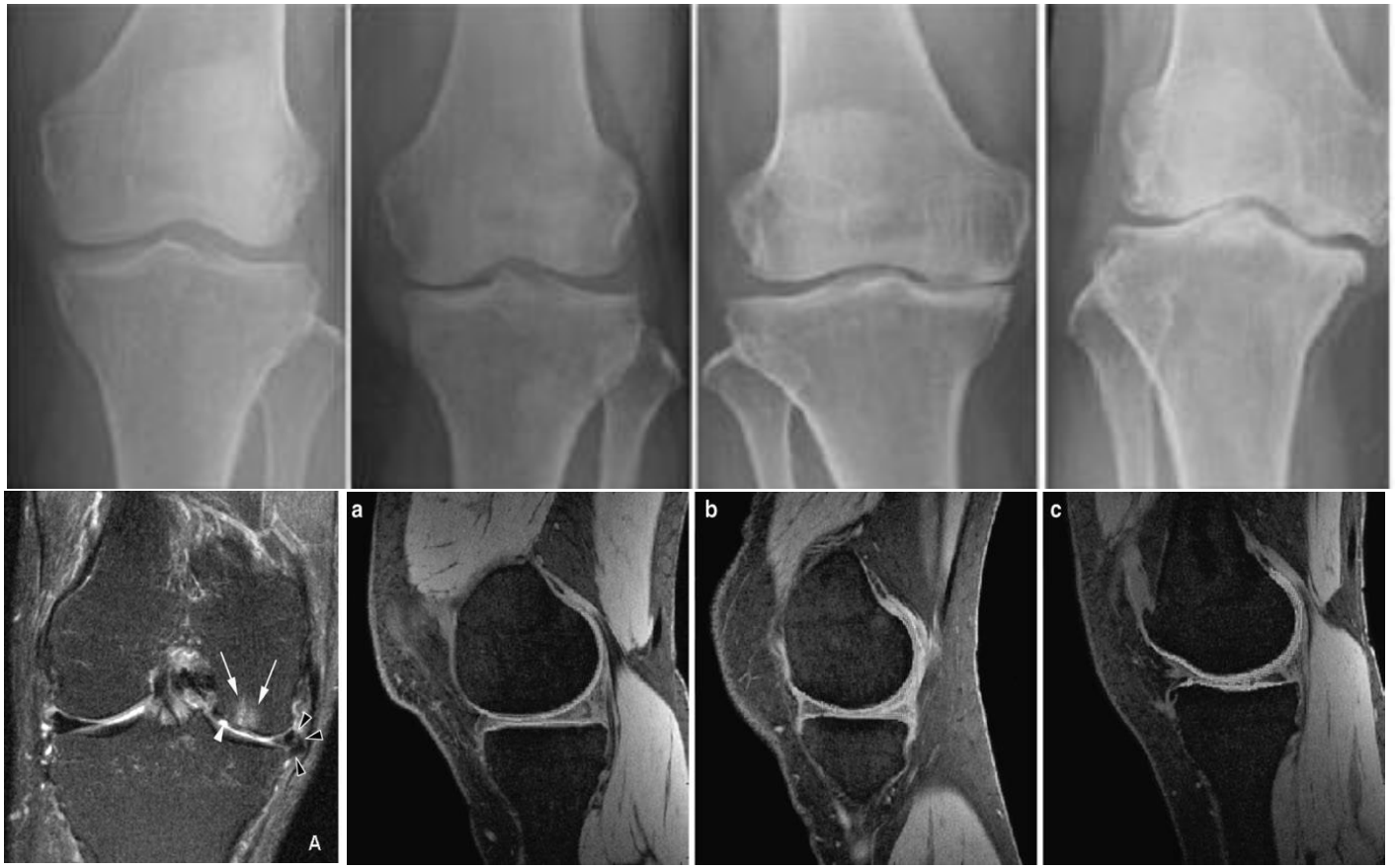


Direct costs of OA



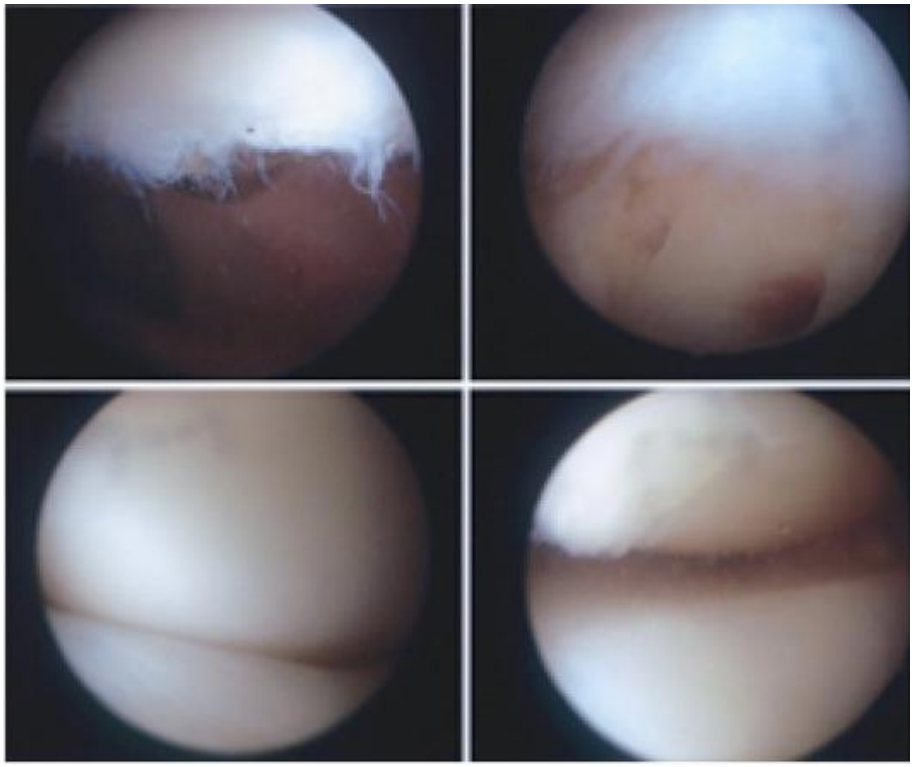
David et al., doi: 10.1038/nrrheum.2014.44

Clinical imaging modalities in OA : X-ray and MRI

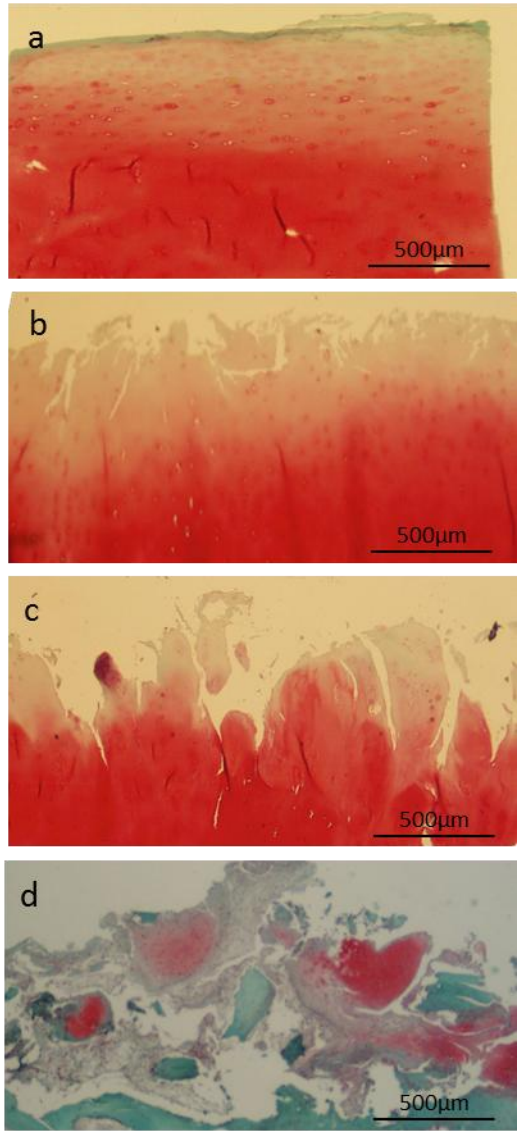


Multiple abnormalities | Healthy control | Mild OA | Severe OA

Clinical Imaging modalities in OA : Arthroscopy



Histo-pathology in OA

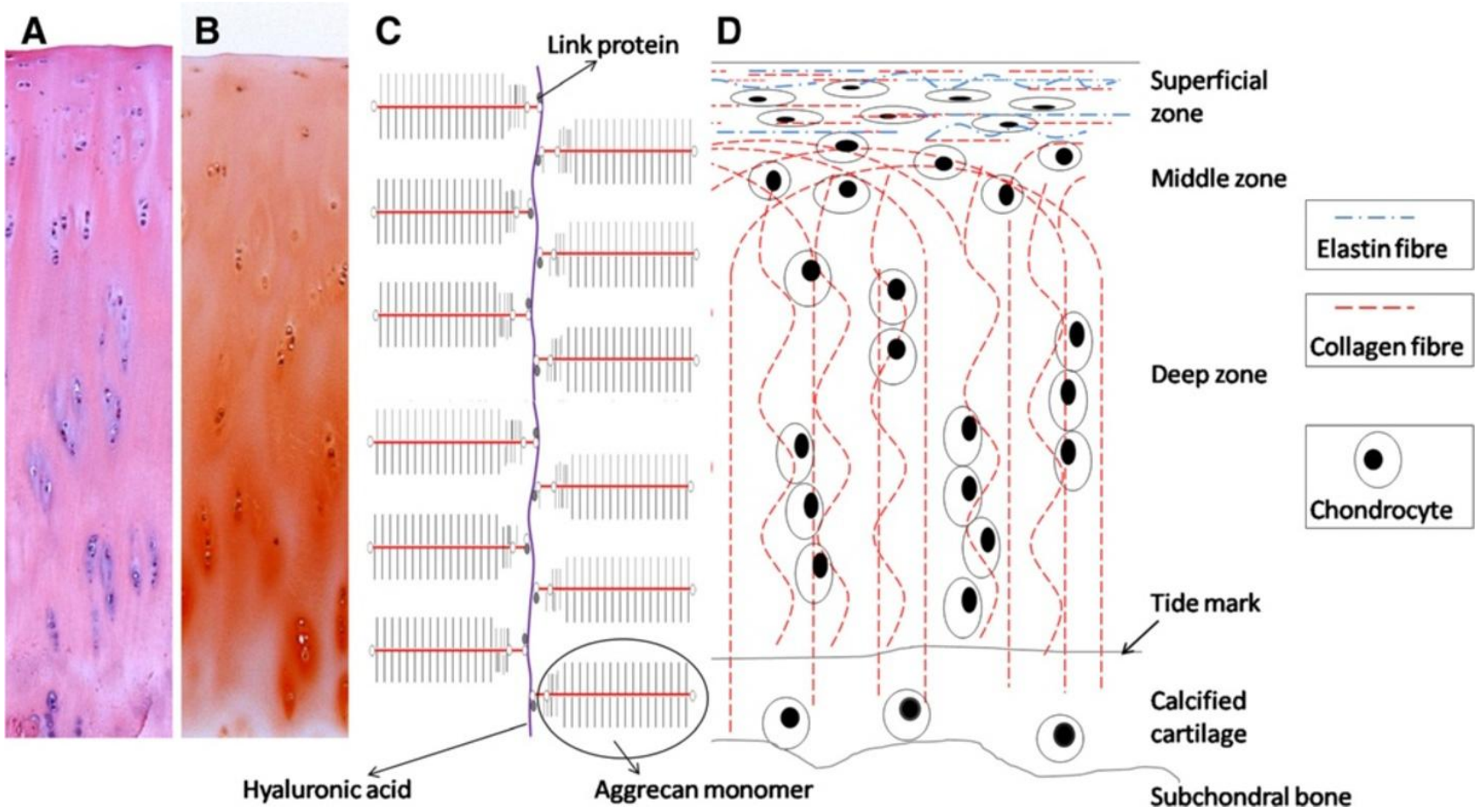


Histological image of osteoarthritic cartilage stained by Safranin-O/Fast Green. Distribution of proteoglycan is illustrated in orange/red

(a) ICRS Grade I
(b) ICRS Grade II
(c) ICRS Grade III
(d) ICRS Grade IV

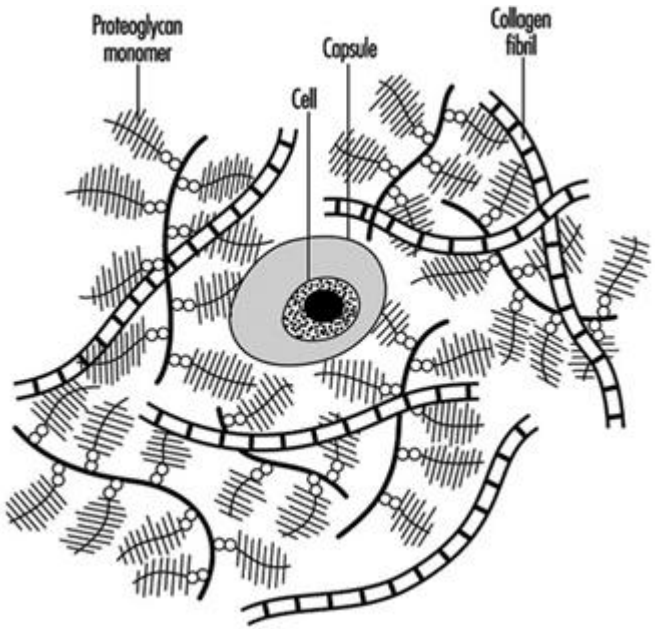
Rajesh et al., Anal Bioanal Chem (2015) 407: 8067

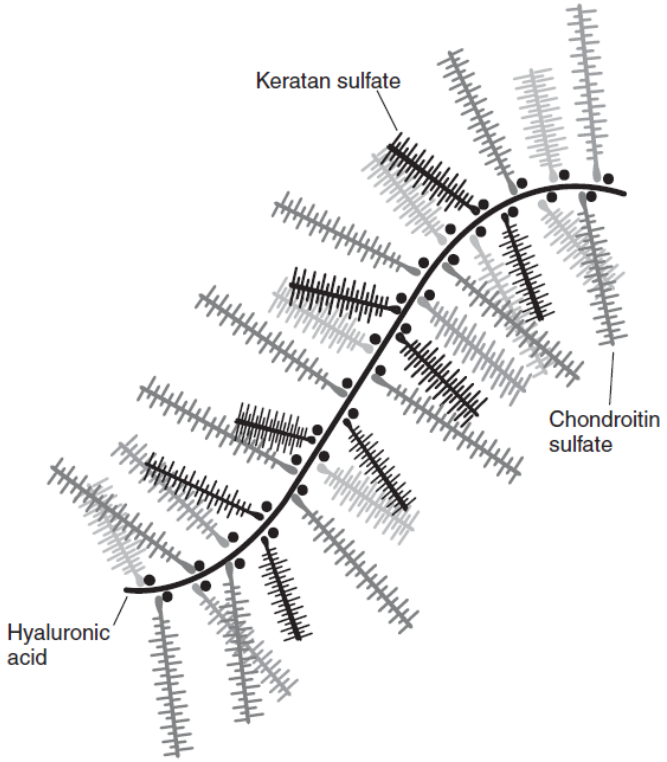
Zonal organization of articular cartilage



He et al. Arthritis Research & Therapy 2014, 16:205

Composition of articular cartilage



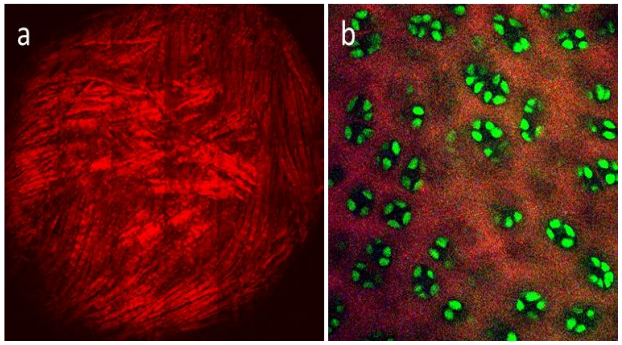


Cartilage -------> Collagen + Proteoglycan + Chondrocytes

Role of Multiphoton Microscopy in the investigation of OA

Table-I: A comparison of different imaging modalities

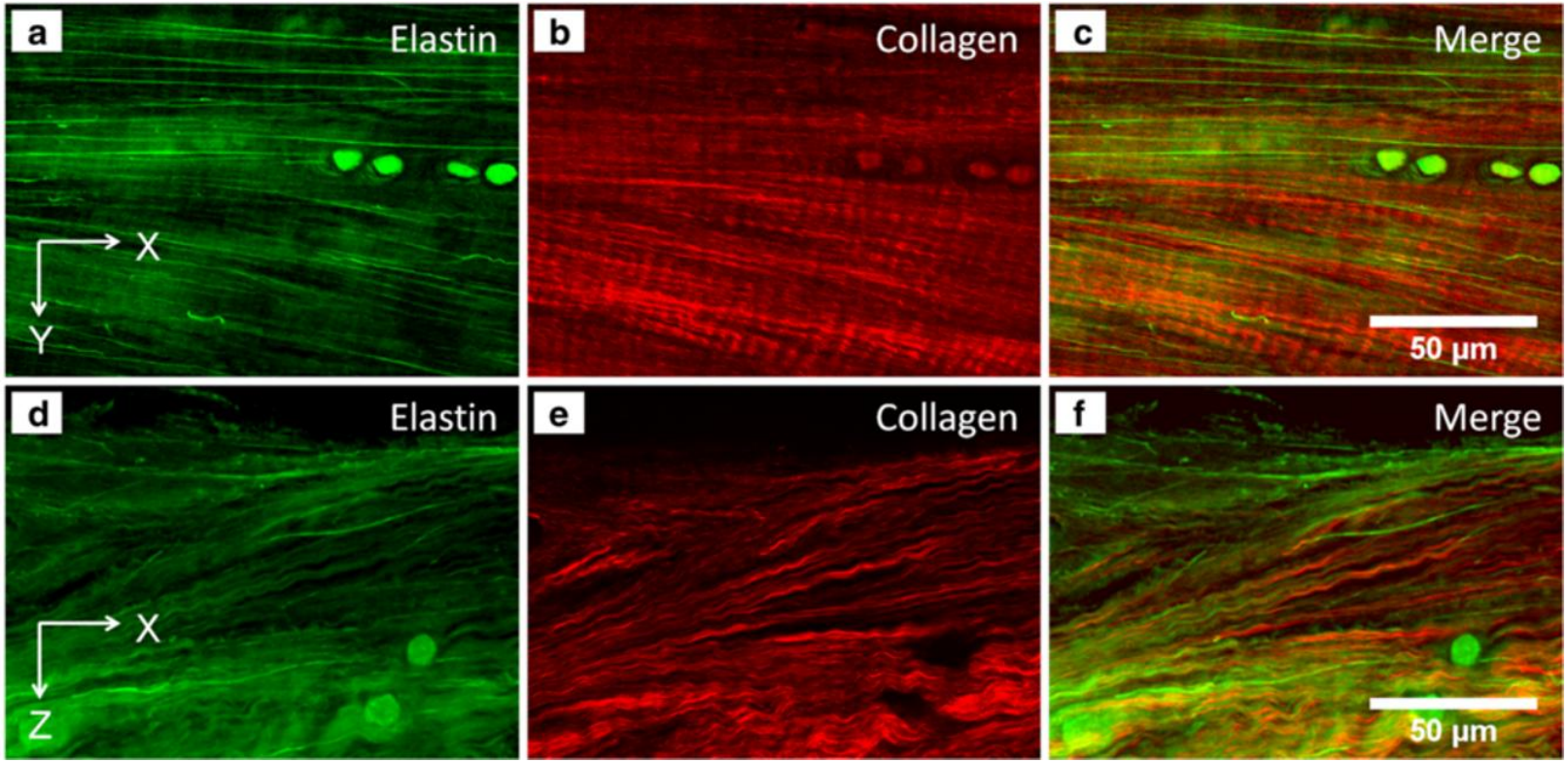
Imaging modality	Imaging depth	Resolution
Confocal microscopy	~ 0.2 mm	~ 1 µm
Two photon microscopy	~ 0.5 mm	~ 1 µm
Optical coherence tomography	~ 1-2 mm	~ 10 µm
Ultrasound	~ 60 mm	~ 150 µm
High resolution CT	Whole joint	~ 300 µm
MRI	Whole joint	~ 1 mm



a. SHG image **b**. SHG (red) and TPEF (green) images

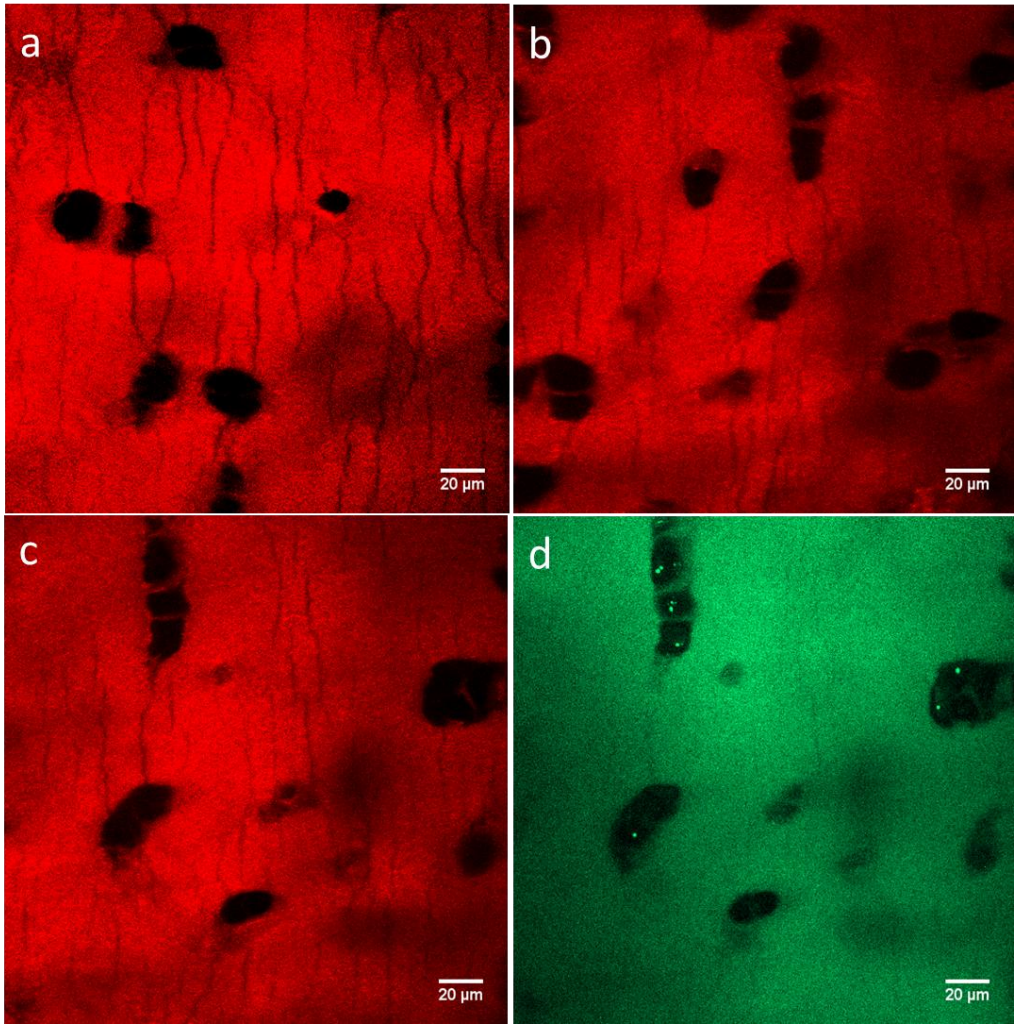
- Degradation of articular cartilage is directly associated with progression of OA.
- NLOM utilizes endogenous optical signals
- Better cell viability, less photo-degradation and improved depth penetration
- Structural and/morphological modifications in the collagen network
- Identification of different types of collagen fibers
- Inherent 3-D optical sectioning
- Chondrocytes morphology/distribution in the lacuna
- Potential of *in-vivo* investigation

Second-harmonic generation (SHG) images of collagen and its relation to elastin fibers.



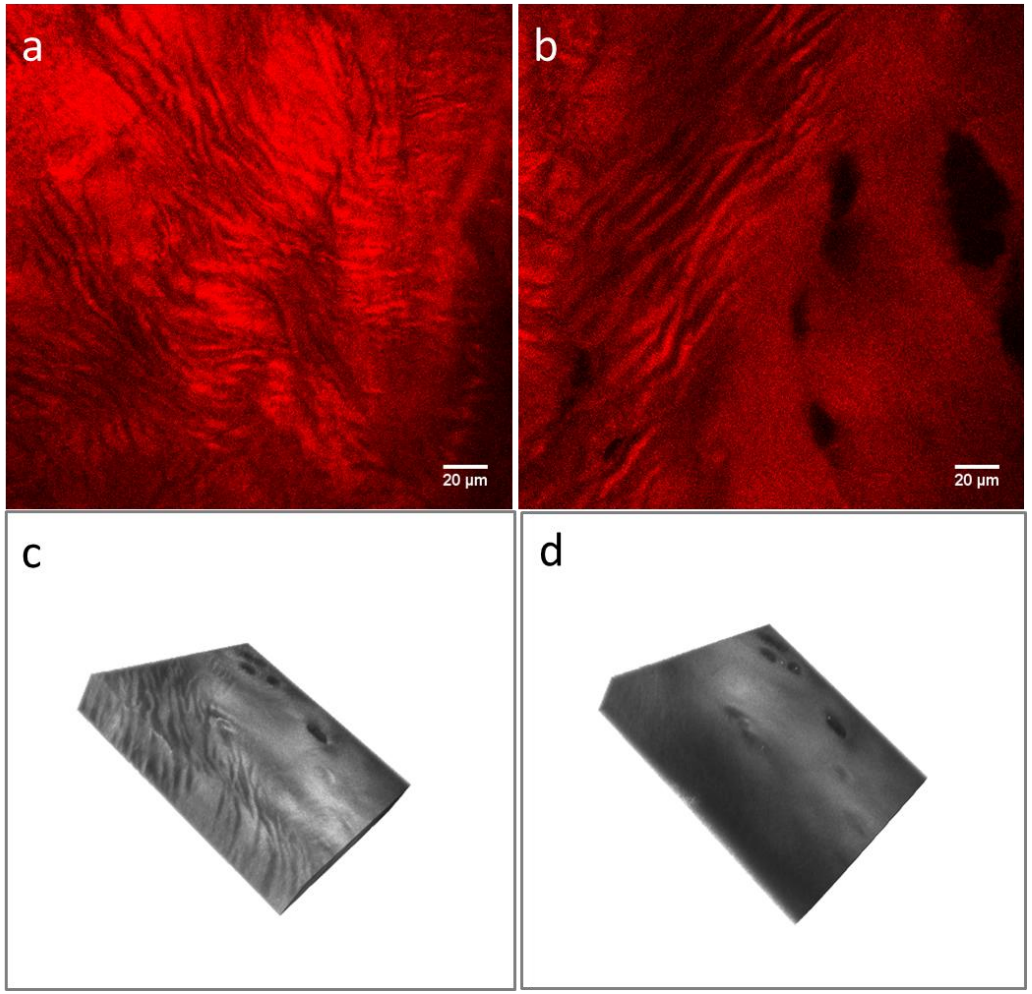
He et al. Arthritis Research & Therapy 2014, 16:205

Second-harmonic generation (SHG) and Two-photon fluorescence (TPF) images of early stage osteoarthritic cartilage



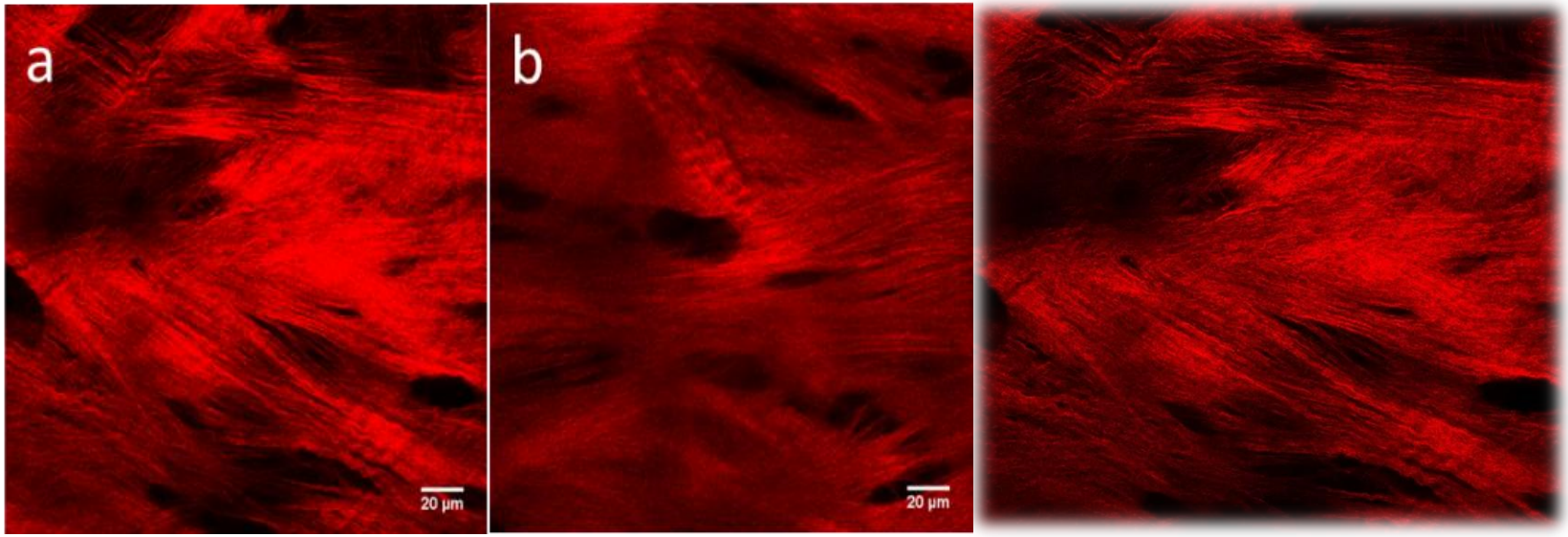
Rajesh et al., Biomed Opt Express. 2015 Apr 27;6(5):1895-903

Second-harmonic generation (SHG) and Two-photon fluorescence (TPF) images of early stage osteoarthritic cartilage



Rajesh et al., Biomed Opt Express. 2015 Apr 27;6(5):1895-903

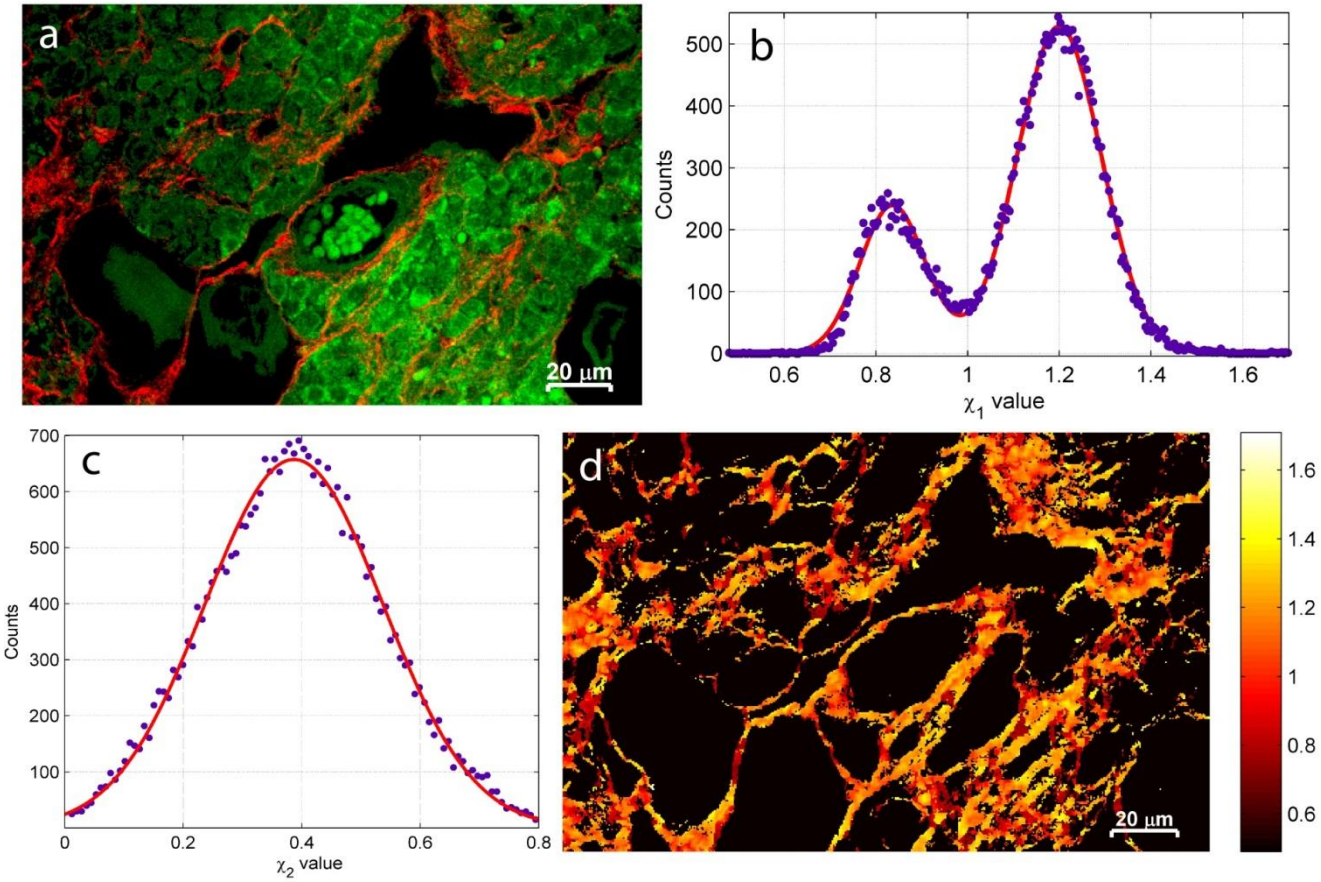
Second-harmonic generation (SHG) images of early stage osteoarthritic cartilage: evidence of superficial layer



SHG images of ICRS Grade-I osteoarthritic cartilage that shows superficial layer at depth (a) 5µm (b) 15µm.

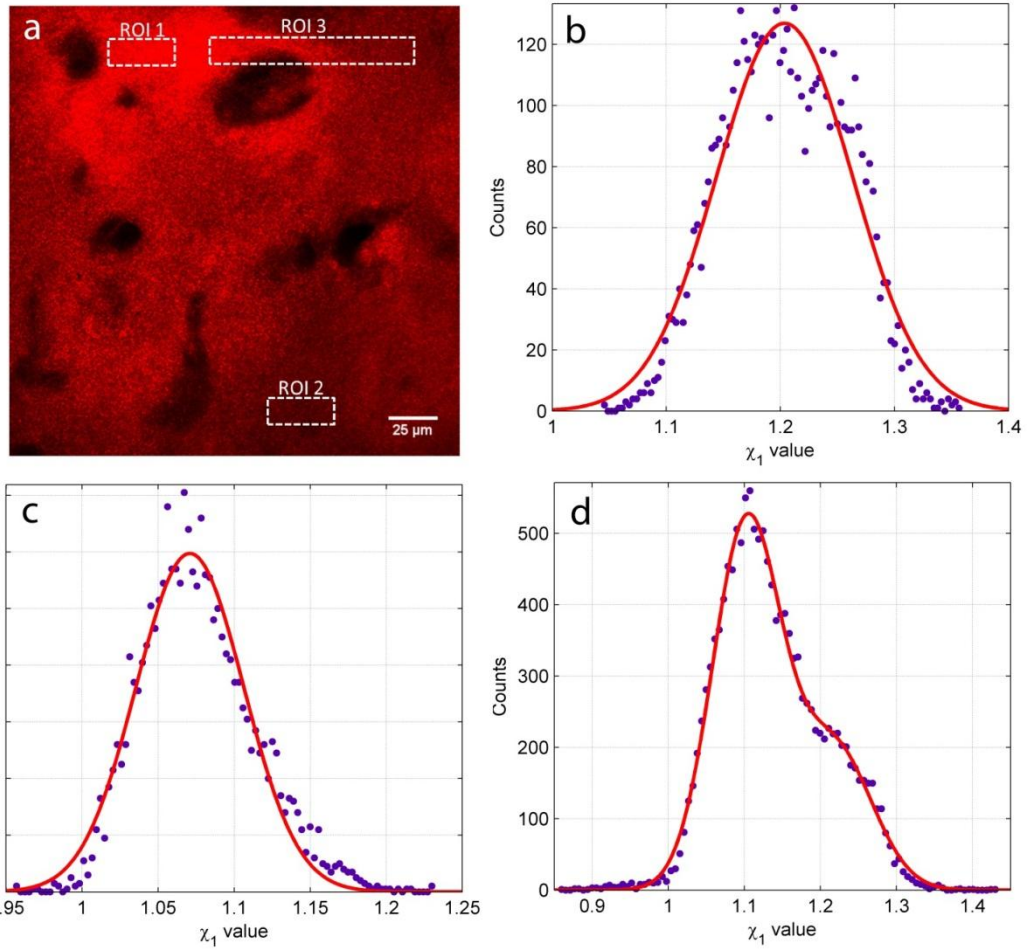
3D-Optical sectioning

Polarization-resolved second harmonic generation (p-SHG) microscopy



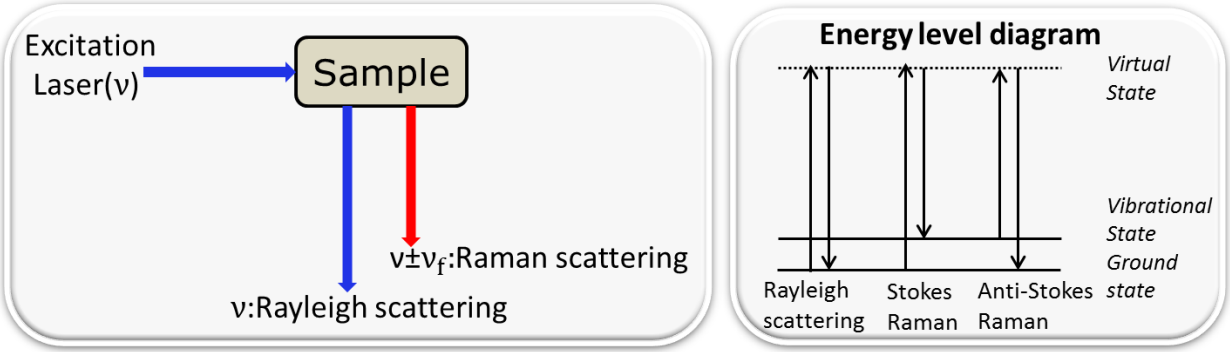
Rajesh et al., J. Biophoton, 8: 730–739 (2015).

Polarization-resolved second harmonic generation (p-SHG) microscopy Osteoarthritic cartilage



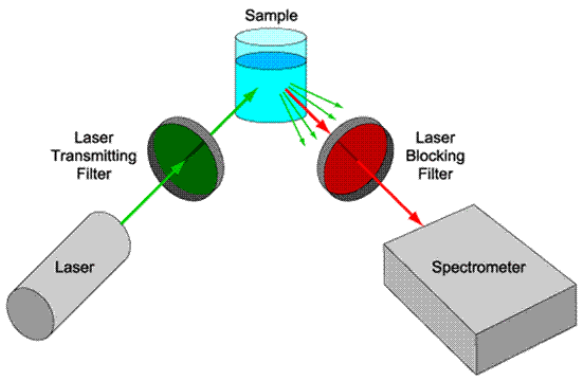
Rajesh et al., J. Biophoton, 8: 730–739 (2015).

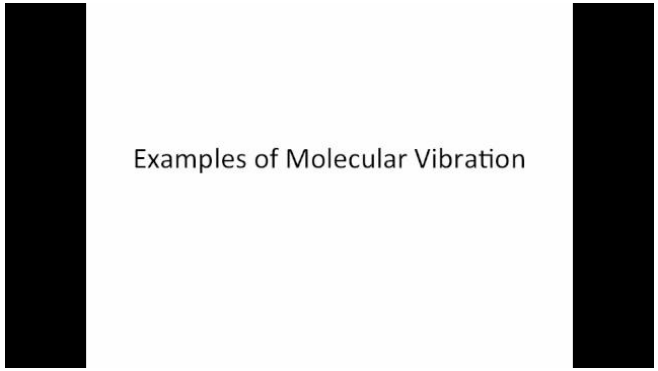
Bio-spectroscopy-Raman spectroscopy



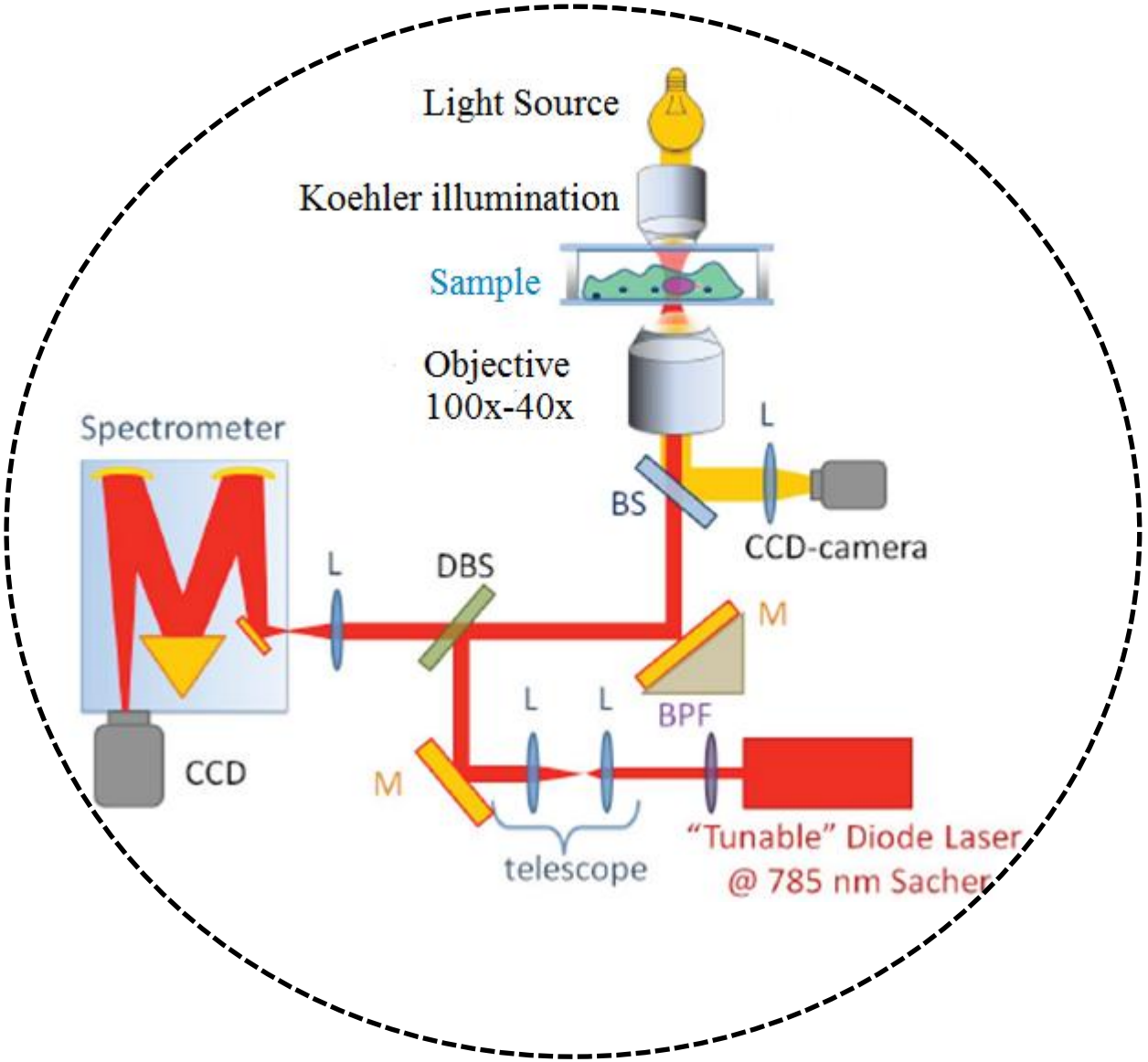
The different possibilities of light scattering: Rayleigh scattering, Stokes Raman scattering and anti-Stokes Raman scattering.

$$P = \alpha_0 E_0 \cos(2\pi\nu t) + \frac{1}{2}\left(\frac{\partial\alpha}{\partial r}\right)_0 r_0 E_0 \left[\cos\{2\pi(\nu+\nu_f)t\} + \cos\{2\pi(\nu-\nu_f)t\}\right]$$

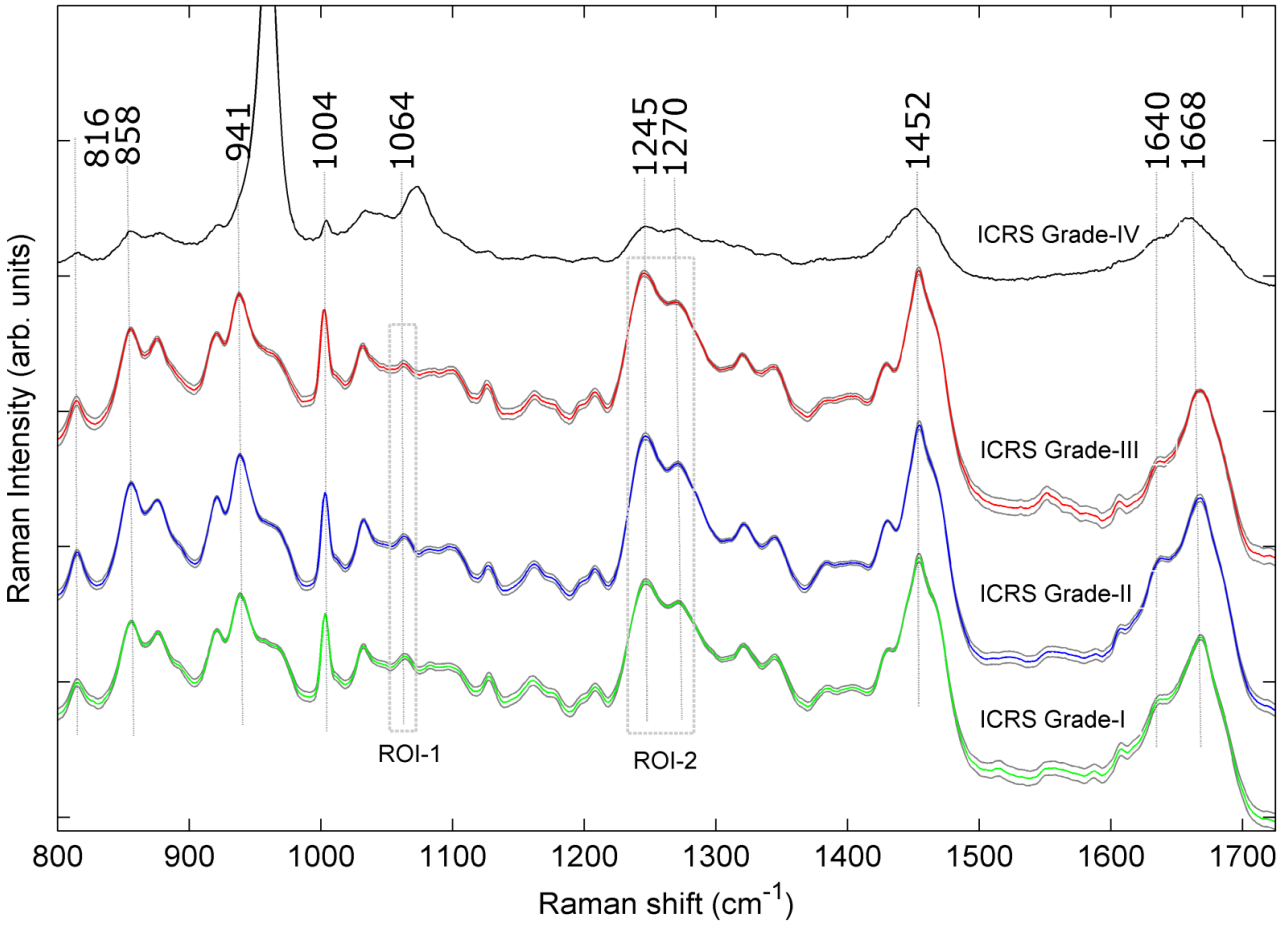




Experimental set-up



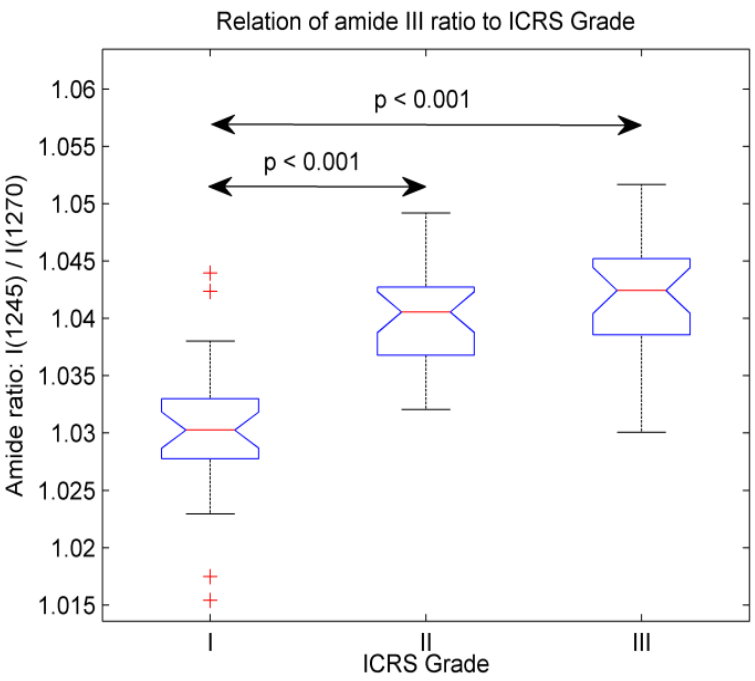
Raman spectroscopy of osteoarthritic cartilage



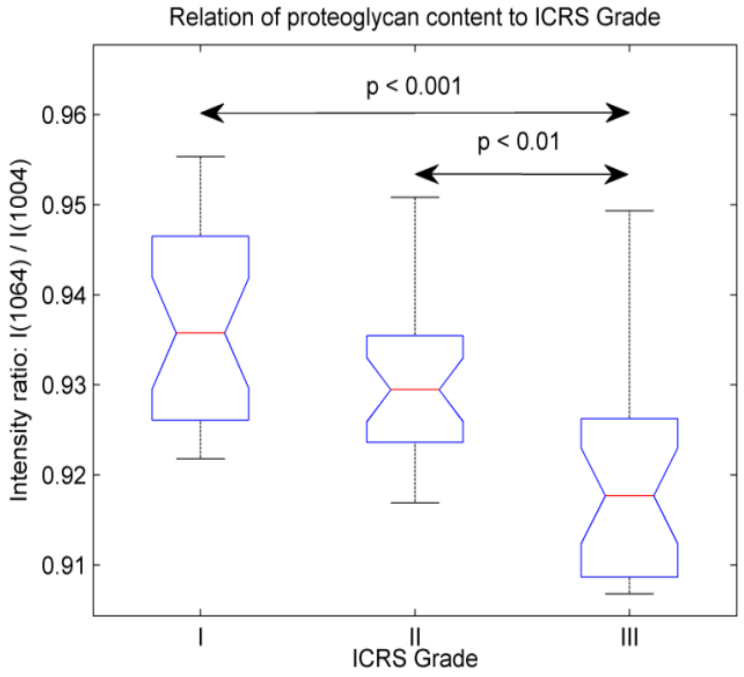
Mean (n=108) normalized Raman spectra obtained from ICRS Grade I, II, III, and IV tissues

Rajesh et al., Anal Bioanal Chem (2015) 407: 8067

Raman spectroscopy of osteoarthritic cartilage



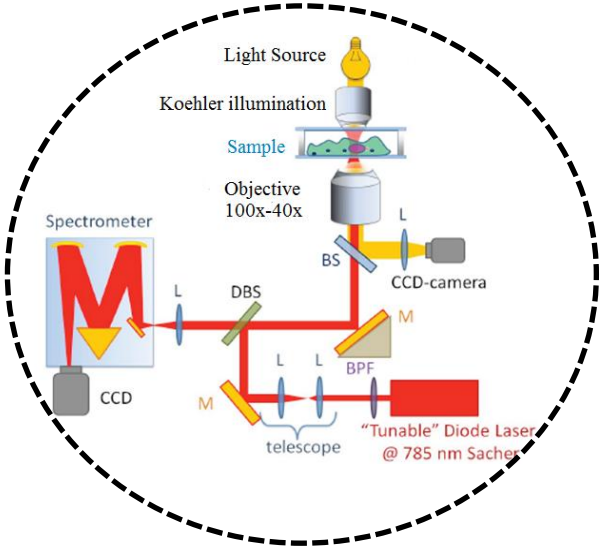
Comparison of relative amide III content in tissues of different grades of osteoarthritis. The dependence of **the ratio of random vs. ordered protein coil content** is shown as a function of ICRS grade. The symbol '+' represents outliers in the data set.

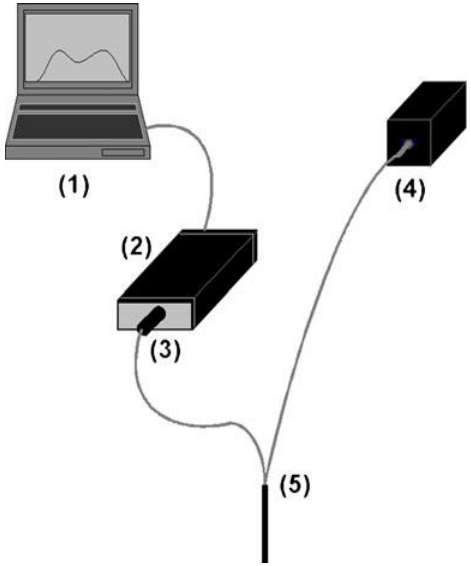


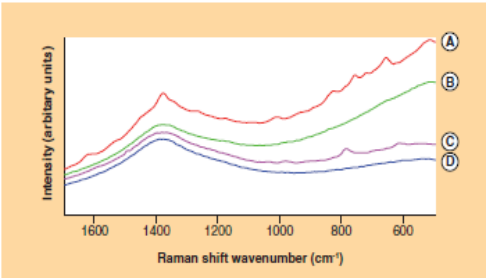
A relative comparison of **proteoglycan contents** in tissues of different grades of osteoarthritis. The dependence of the proteoglycan content inside the cartilage matrix is shown as a function of ICRS grade of osteoarthritis.

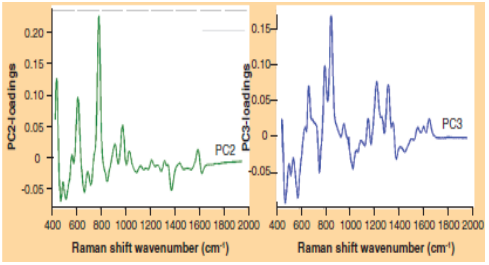
Rajesh et al., Anal Bioanal Chem (2015) 407: 8067

Prospect of endoscopic Raman probe









Potential and challenges

Potential of developing second-harmonic generation arthroscopy

Beneficial to early diagnosis of OA.

- During the early stage of OA, collagen content is initially maintained, but collagen organization is severely perturbed.

Capability for distinguishing different types of collagen (How?)

- Collagen Type-I
- Collagen Type-II
- Collagen Type-III

Challenges for developing second-harmonic generation arthroscopy

Minimize the SHG microscope

- Long and thin probe instead of objectives
- Laser and the cooling system
- Excitation and emission optical path
- Incorporation of polarization optics
- Magnification choices for researchers/clinicians

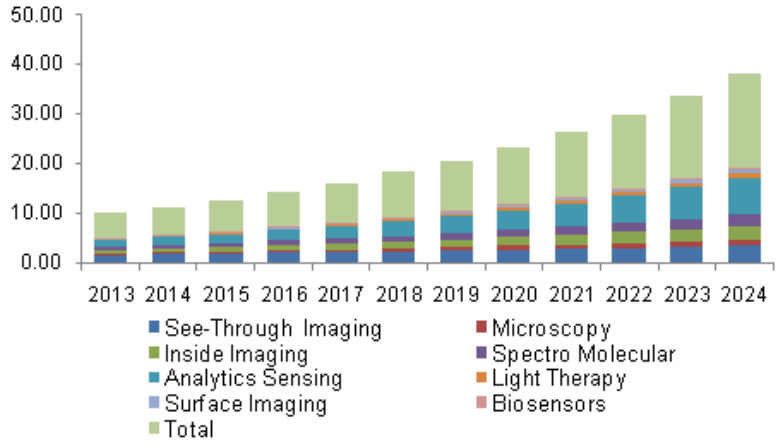
Market prediction

The European Commission identified photonics and imaging as technologies of exceptional importance for a knowledge-based economy, with the photonics industry in Europe worth approximately €58 billion.

Source: labnews.co.uk/features/biophotonics

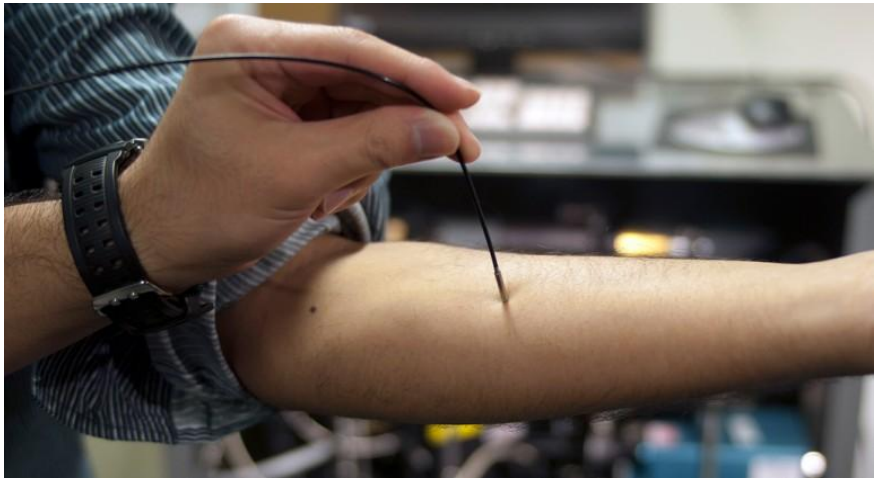
European Commission

Asia Pacific Biophotonics Market by Application, 2013 - 2024 (USD Billion)



Source: Grand View Research, Inc., CA, USA

Source: Global Industry Analysis, Inc. San Jose, CA

Conclusion

Prospect for the development of non-invasive imaging/diagnostic techniques